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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,178	02/12/2002	David J. Eyre	7475-69889	5007

49437 7590 09/05/2006

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INDIANAPOLIS, IN 46204

EXAMINER
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SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 09/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/074,178

Applicant(s)

EYRE ET AL.

Examiner

Carolyn L. Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 18-25 is/are pending in the application.
- 4a) Of the above claim(s) 24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 18-23 and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission, filed 6/16/06, has been entered.

Amended claims 18-21 and new claim 25, filed 6/16/06, are acknowledged. Claim 24 remains withdrawn as being drawn to a non-elected specie.

Claims herein under examination are 18-23 and 25.

### *Claim Rejections - 35 USC § 112, Second paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-23 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites the terms "using" (lines 9 and 11-12) and "to use" (lines 10, 13) and claim 25 recites "to use" (lines 10 and 11) and "using" (line 10) which are vague and indefinite. It is unclear what steps or data manipulations are intended to be encompassed by the various "uses" of algorithms and fluorescent values. Clarification of this issue via clearer claim wording is requested. Claims 19-23 are also rejected due to their dependency from claim 18.

*Claim Rejections – 35 USC §102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
- (f) he did not himself invent the subject matter sought to be patented.

Claims 18, 22, and 23 are rejected under 35 U.S.C. 102(e)(2) and 102(f) as being anticipated by Wittwer (P/N 6,387,621 B1).

Wittwer discloses a system with a rapid thermal cycling device using capillary tubes and hot air temperature control (col. 4, line 66 to col. 5, line 2) which represents the instrument in instant claim 18, 22, and 23. Wittwer discloses analyzing a sample for the presence of a nucleic acid using polymerase chain reaction and a fluorescent detecting entity (col. 1, lines 13-18) as stated in the preamble of instant claim 18. Wittwer discloses amplification with product analysis for “real-time” PCR in the same instrument (col. 1, lines 25-40). Wittwer discloses the LightCycle<sup>™</sup> as a rapid temperature cycler with a fluorimeter (col. 5, lines 42-44) which is a PC-based instrument with integrated algorithms in the LightCycle<sup>™</sup> platform (col. 5, lines 45-57) which represents a temperature cycler, fluorimeter, and processor, as stated in instant claim 18. Wittwer discloses determining the presence of a nucleic acid by analyzing fluorescent entity measurements capable of detecting the nucleic acid and its number during amplification via

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slope analysis of fluorescence intensity (col. 2, lines 27-52) and a fluorescent entity providing a signal related to the quantity of the nucleic acid (claim 1), as stated in instant claim 18. Wittwer discloses comparing fluorescent values after each amplification cycle (col. 2, lines 45-52) and detection via a fluorimeter (col. 5, lines 42-44). Wittwer discloses the automated process involving a thermal cycler having a sensor for reporting fluorescence values as a function of cycle number and a processor programmed with an algorithm to process values and report a positive or negative result (col. 2, lines 53-58). Wittwer discloses initiation of the analysis algorithm prior to the completion of temperature cycling (col. 2, first paragraph), as stated in instant claim 18. Wittwer discloses first derivative estimate, second derivative estimate, and confidence band factor as well as using an algorithm where the fluorescent values determine the first and second derivatives (i.e. first and second scores) which correspond to cycle numbers and assigning derivative values to the certain cycle numbers after which a baseline, baseline region and confidence intervals for a predicted negative test point are determined (i.e. Figure 7; col. 7, line 46 to col. 8, line 67; col. 3, lines 22-30), a composite score denoted by a rightmost large black circle on Figures 7-11), and using a test point cycle to determine against the baseline for determining a positive or negative result (col. 8, lines 45-52) which represents obtaining first, second, and composite scores to determine whether the sample is positive or negative, as stated in instant claim 18. Wittwer discloses using a confidence interval test (col. 8, lines 53-67). Wittwer discloses accounting for background fluorescence and comparing fluorescent values to a baseline fluorescent region (col. 2, lines 45-47). Wittwer discloses sample temperature tests using capillaries with forced air heating allowing precise control of temperature as well as using a rapid temperature cycler with a fluorimeter (col. 5, lines 8-44). Wittwer discloses analysis

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occurring concurrently with amplification to decrease sample handling, save time, and reduce contamination risks (col. 1, lines 29-38). Wittwer discloses reporting values as a function of cycle number and reporting results (col. 2, lines 53-58) and analyzing fluorescent measurements over a wide range of amplification cycles (col. 6, lines 48-63). Wittwer discloses a maximum to baseline comparison (col. 6, first paragraph). Wittwer discloses determining the test point cycle for determining a positive or negative result which may be the last cycle for a curve not well behaved (col. 8, lines 45-48).

Thus, Wittwer anticipates the limitations of instant claims 18, 22, and 23.

Applicant argues that amended claims 18, 22, and 23 require that the processor be programmed to use at least two different tests employing two different algorithms, with each test producing a score. This statement is found unpersuasive as amended claim 18 only recites a “first algorithm” which does not require the use of two different algorithms. Applicant argues that Wittwer does not describe the multi-test analysis specified in amended claims 18, 22, and 23. This statement is found unpersuasive as the formation of derivatives from the fluorescent values, as disclosed by Wittwer ((i.e. Figure 7; col. 7, line 46 to col. 8, line 67; col. 3, lines 22-30) represent first and second scores from tests. Applicant reiterates the argument regarding employing two different algorithms that was previously found unpersuasive, as stated above.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 19-21 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wittwer (P/N 6,387,621 B1) as applied to claims 18, 22, and 23 above, and further in view of Schork et al. (P/N 6,291,182 B1).

Wittwer discloses the limitations of instant claims 18, 22, and 23, as set forth in the 35 USC 102 rejection above. Wittwer does not teach all of the plurality of tests as stated in instant claims 19-21 and 25.

Schork et al. describe methods, software, and apparatus for determining the presence of a gene with a detectable trait in a genomic region (presence of a nucleic acid in a sample) (abstract). Schork et al. describe using a Perkin Elmer 9600 Thermocycler to perform amplification of nucleic acids (col. 47, lines 1-6). Schork et al. describe performing 40 cycles with 30 seconds at 95 degrees Celsius, 1 minute at 54 degrees Celsius and 30 seconds at 72 degrees Celsius (col. 47, lines 2-6) which represent rapid thermal cycling, as stated in instant claim 22. Schork et al. describe using a fluorimeter and Picogreen (fluorescence) to determine quantities of amplification products (col. 47, lines 7-9). Schork et al. describe excluding artifacts

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due to background noise by comparing two DNA strands (col. 47, lines 29-34) which represents a signal-to-noise ratio test, as stated in instant claims 19 and 25. Schork et al. describe using a variety of mathematic analysis tests, including Expectation-Maximization method (Maximum to Baseline Comparison Test) (col. 2, line 6), Wilcoxon rank test (function ordering test) (col. 2, line 62), Kolmogorov-Smirnov test (efficiency test using normal distribution) (col. 2, line 65), chi-square test (confidence interval test) (col. 2, line 50), and nonparametric tests (Last Rise Test) (Fig. 24), as stated in instant claims 19, 20, 21, and 25. Schork et al. describe performing linkage analysis based upon establishing a correlation between transmission of genetic markers and that of a specific trait throughout generations within a family and statistical methods for determination of the likelihood that the marker and trait are segregating independently (col. 18, lines 39-64) which represents a type of Channel Consistency Test where the channel consistency is represented by the consistent flow (presence) or lack thereof of the marker and trait transmission throughout generations, as stated in instant claim 20.

Wittwer and Schork et al. provide methods and devices for determining the presence of a nucleic acid in a sample (abstract of each). Wittwer states there is a need for algorithms for detection, quantification, and genotyping (col. 2, lines 5-6). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Wittwer by analyzing data with detection analysis tests as taught by Schork et al. wherein the motivation would have been to process data occurring during amplification including concomitant analysis results to modify temperature cycling as well as to acquire additional data during the latter stages of the amplification procedure to optimize amplification protocol and data quality, as stated by Wittwer (col. 2, lines 8-13).



Thus, Wittwer, in view of Schork et al., make obvious the instant invention.

Applicant summarizes amended claim 18. Applicant argues that Wittwer does not suggest a processor programmed to initiate multiple algorithms during PCR. This statement is found unpersuasive as Wittwer discloses amplification with product analysis for “real-time” PCR in the same instrument (col. 1, lines 25-40). Furthermore, Wittwer discloses the LightCycle<sup>TM</sup> as a rapid temperature cycler with a fluorimeter (col. 5, lines 42-44) which is a PC-based instrument with *integrated algorithms* in the LightCycle<sup>TM</sup> platform (col. 5, lines 45-57) which represents a temperature cycler, fluorimeter, and processor, as stated in instant claim 18.

Applicant argues that the processor does not generate a composite score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid. This statement is found unpersuasive as “composite score” was broadly and reasonably interpreted due to the lack of a clear and concise definition in the originally filed application. Furthermore, it is noted that Wittwer discloses a positive or negative result (i.e. col. 2, lines 53-58) which reads upon the rejected limitation. Applicant’s argument regarding Wittwer not addressing making indeterminate calls is found unpersuasive as the claim language does not require that all three determinations be made, but rather “positive, negative, OR indeterminate”. It is reiterated that Wittwer discloses positive and negative determinations (i.e. col. 2, lines 53-58). Applicant summarizes the Schork et al. prior art. Applicant argues that the statistical tests described in the Schork et al. patent have nothing to do with the PCR-based assays. This statement is found unpersuasive as the statistical tests encompass the tests recited in instant claims 19-21 and 25. Applicant argues that Schork et al. do not suggest initiating analysis algorithms prior to

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completion of temperature cycling or obtain composite scores. These statements are found unpersuasive as Wittwer discloses these limitations. Applicant is reminded that all limitations in a 35 USC 103 rejection need not come from a single reference, which is why this is a 35 USC 103 rejection as opposed to a 35 USC 102 rejection. Applicant notes that Wittwer does not teach all of the plurality of tests in instant claims 19-21. However, it is noted that Wittwer, in view of Schork et al., teach all of these tests (as summarized in the 35 USC 103 rejection above). Applicant argues that column 47, lines 29-43, of Schork et al. fails to indicate a value or score. This statement is found unpersuasive as Wittwer discloses scores and values for the 35 USC 103 rejection.

### ***Conclusion***

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

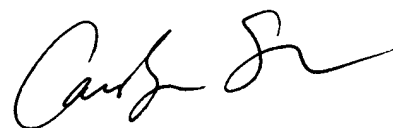
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721.. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Yolanda Chadwick whose telephone number is (571) 272-0514.

August 28, 2006

A handwritten signature in black ink, appearing to read 'Carolyn Smith', with a stylized flourish at the end.

Carolyn Smith  
Examiner  
AU 1631